

(19)



Europäisches Patentamt

European Patent Office

Office européen des brevets



(11)

EP 0 850 926 A3

(12)

## EUROPEAN PATENT APPLICATION

(88) Date of publication A3:  
16.06.1999 Bulletin 1999/24

(51) Int. Cl.<sup>6</sup>: C07C 405/00, A61K 31/557

(43) Date of publication A2:  
01.07.1998 Bulletin 1998/27

(21) Application number: 97122702.0

(22) Date of filing: 22.12.1997

(84) Designated Contracting States:  
AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC  
NL PT SE  
Designated Extension States:  
AL LT LV MK RO SI

(30) Priority: 26.12.1996 JP 34861496  
26.03.1997 JP 7405497  
27.06.1997 JP 17247797

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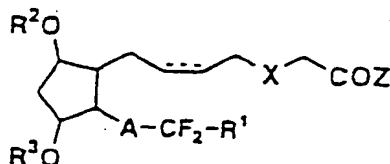
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## (54) Difluoroprostaglandin derivatives and their use

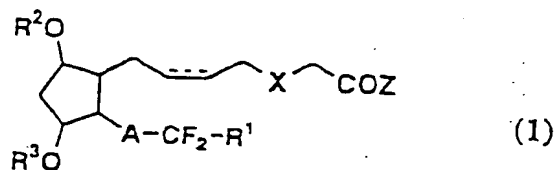
(57) A fluorine-containing prostaglandin derivative of the formula (1) or a salt thereof, and a medicine containing it, particularly, as a preventive or therapeutic medicine for an eye disease:



(1)

wherein A is a vinylene group or the like, R<sup>1</sup> is an aryloxyalkyl group or the like, R<sup>2</sup> and R<sup>3</sup> are hydrogen atoms or the like, and Z is OR<sup>4</sup>, therein OR<sup>4</sup> is a hydrogen atom or an alkyl group or the like.

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10 wherein A is an ethylene group, a vinylene group, an ethynylene group,  $-OCH_2-$  or  $-SCH_2-$ ,

$R^1$  is a substituted or unsubstituted  $C_{3-8}$  alkyl group, a substituted or unsubstituted  $C_{3-8}$  alkenyl group, a substituted or unsubstituted  $C_{3-8}$  alkynyl group, a substituted or unsubstituted  $C_{3-8}$  cycloalkyl group, a substituted or unsubstituted aralkyl group or a substituted or unsubstituted aryloxyalkyl group,  
 15 each of  $R^2$  and  $R^3$  which are independent of each other, is a hydrogen atom or an acyl group, or forms a single bond together with Z,

X is  $-CH_2-$ ,  $-O-$  or  $-S-$ ,

Z is  $-OR^4$ ,  $-NHCOR^5$ ,  $-NHSO_2R^6$  or  $-SR^7$ , or forms a single bond together with  $R^2$  or  $R^3$ ,

20 each of  $R^4$ ,  $R^5$ ,  $R^6$  and  $R^7$  which are independent of one another, is a hydrogen atom, an alkyl group, an alkenyl group, an alkynyl group, a cycloalkyl group, an aryl group or an aralkyl group,  
 and a dual line consisting of solid and broken lines is a single bond, a cis-double bond or a trans-double bond.

2. The compound according to Claim 1, wherein A is an ethylene group or a vinylene group.

25 3. The compound according to Claim 1 or 2, wherein X is  $-CH_2-$ .

4. The compound according to any one of Claims 1 to 3, wherein Z is  $-OR^4$ .

5. The compound according to any one of Claims 1 to 4, wherein  $R^1$  is a substituted or unsubstituted aryloxyalkyl group.  
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6. The compound according to Claim 5, wherein  $R^1$  is a phenoxyethyl group, a 3,5-dichlorophenoxyethyl group or a 3-chlorophenoxyethyl group.

35 7. 16-Phenoxy-15-deoxy-15,15-difluoro-17,18,19,20-tetranorprostaglandin  $F_{2\alpha}$ , 16-(3-chlorophenoxy)-15-deoxy-15,15-difluoro-17,18,19,20-tetranorprostaglandin  $F_{2\alpha}$ , 16-phenoxy-15-deoxy-15,15-difluoro-13,14-dihydro-17,18,19,20-tetranorprostaglandin  $F_{2\alpha}$  or an alkyl ester or a salt thereof.

8. A medicine containing the compound according to any one of Claims 1 to 7 as an active ingredient.  
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9. A preventive or therapeutic medicine for an eye disease containing the compound according to any one of Claims 1 to 7 as an active ingredient.

45 10. The medicine according to Claim 9, wherein the eye disease is glaucoma or ocular hypertension.



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# EUROPEAN SEARCH REPORT

Application Number  
EP 97 12 2702

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E	--- WO 98 12175 A (MATSUMURA YASUSHI ;MORI NOBUAKI (JP); NAKANO TAKASHI (JP); SAKATA) 26 March 1998 * claims *	1-10	
The present search report has been drawn up for all claims			TECHNICAL FIELDS SEARCHED (InCL6)
Place of search THE HAGUE		Date of completion of the search 22 April 1999	Examiner BERTE, M
<p>CATEGORY OF CITED DOCUMENTS</p> <p>X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document</p> <p>T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons &amp; : member of the same patent family, corresponding document</p>			

EPO FORM 1503 03.92 (P0401)

**ANNEX TO THE EUROPEAN SEARCH REPORT  
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This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report.  
The members are as contained in the European Patent Office EDP file on  
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For more details about this annex : see Official Journal of the European Patent Office, No. 12/82